substantial release of the butorphanol tartrate capable of intraoral administration during intraoral administration thereby informing the patient that it is time to orally ingest the remaining second part of the composition containing the rofecoxib capable of oral administration.

Remarks

Amendments to the claims

Claims 1, 29, 30 and 32 have been amended to clarify that the outer layer dissolves or disintegrates in a patient's mouth (Support is found at page 15, lines 5-18; page 18, lines 25-26) and that the active ingredient is absorbed sublingual or buccally in a therapeutically effective level (Support is found at page 7, lines 17-20). Dependent claims were also amended as required to correct antecedent basis.

Restriction Requirement and Election of Species

Claims 30-31, drawn to method of use, have been cancelled as drawn to a non-elected invention.

Claims 4 and 20-21, dependent upon claims under examination, have been withdrawn as drawn to a non-elected species, with the understanding they will be examined if the claims are otherwise determined to be allowable.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 26 was rejected as indefinite. The objected-to recitation "has a first pass metabolism" has been amended to more clearly recite "is metabolized in a first pass" .One of ordinary skill in the art would recognize that the term "first pass" refers to "metabolism in the liver when an active ingredient is administered orally." (see, Kvetina, et al., "Experimental Goettingen minipig and beagle dog as two species used in

bioequivalence studies for clinical pharmacology (5-aminosalicylic acid and atenolol as model drugs)" in Gen Physiol Biophys 18 (Spec.):80-5 (1999)) and the enclosed excerpt from "Medical Pharmacology 2002 Supplemental Handout Dr. Willis, Bioavailability and Apparent Volume of Distribution".

Rejections Under 35 U.S.C. § 102

Claims 1-3, 6, 8-11 and 25-29 were rejected as anticipated under 35 U.S.C. §102(b) by U.S. Patent No. 5,053,032 to Barclay et al. ("Barclay"). Claims 1-3, 5, 7, 10, 14, 16-18, 27 and 29 were rejected as anticipated under 35 U.S.C. §102(b) by U.S. Patent No. 5,558,879 to Chen et al. ("Chen"). Applicants respectfully traverse the rejections if they are applied to the claims as amended.

The Claimed Invention

The claims are drawn to a pharmaceutical composition in unit dosage form for both intraoral and oral administration to a patient, and method of manufacture. The unit dosage form has a first portion which has at least one discrete outer layer that dissolves or disperses in the mouth (sublingual or buccal) containing a therapeutically effective amount of at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level. The unit dosage form has a second portion located within the first portion, which has a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the outer layer has disintegrated or has dissolved intraorally.

Barclay

As the Examiner correctly noted, Barclay describes and claims an osmotic device for controlled delivery of an active beneficial agent into the oral cavity of an animal such as human (col. 4, lines 53-55). An osmotic drug delivery system uses osmotic effect of a material to force out an active agent to be delivered. As such, an osmotic drug delivery system requires an outer coating around the device that is permeable to an aqueous medium but must retain its integrity upon contact with the aqueous medium (see, for example, Carr, "Drug Delivery: A crucial role" in Scrip Magazine, November 1997, at http://www.carr.pair.com/scrip.html; and Dong, et al., "Controlled Release. L-OROS® SOFTCAP™ for Controlled Release of Non-Aqueous Liquid Formulations" in http://www.drugdeliverytech.com/cgi-bin/articles.cgi?idArticle=15). Indeed, Barclay at col. 4, lines 55-58, requires the device to have a wall formed of a material which is permeable to the passage of an external aqueous fluid which is present in the oral cavity.

Accordingly, Barclay does not have an outer layer which dissolves or disperses in the mouth, and therefore does not anticipate the claims.

Chen

Chen describes a controlled release osmotic tablet (col. 3, lines 18-20). The Tablet requires a water soluble osmotic agent (col. 3, lines 27) and is coated with a water **insoluble** polymeric membrane (col. 3, lines 32-33). Again, the Examiner is correct in noting that Chen describes and claims an osmotic drug delivery device.

In contrast the claims define a pharmaceutical unit dosage form which is different from an osmotic delivery device (see the discussion above). In particular, the amended claims more clearly define the outer layer as one which disintegrates or dissolves in the patient's mouth. This feature along clearly distinguishes the device of Chen.

Rejection Under 35 U.S.C. § 103

The Examiner rejected claims 4-5, 7, 12-24, and 32 as obvious under 35 U.S.C. § 103 over Barclay in view of U.S. Pat. No. 4,814,181 to Jordan et al. ("Jordan"). The Examiner further rejected claims 4-5, 7, 12-24, and 32 as obvious over Barclay in view of U.S. Pat. No. 6,004,582 to Faour et al. ("Faour"). The applicants respectfully traverse the rejections if they are applied to the claims as amended.

Barclay, and Chen have been discussed above.

Jordan

Jordan describes an osmotic dosage form for fast delivery of a first agent and slow delivery of a second agent (col. 2, lines 20-68; col. 3, lines 1-29; col. 4, lines 1-28). Further, the dosage form described in Jordan is for gastrointestinal tract delivery (col. 3, lines 9-14). There is no disclosure of intraoral administration.

Accordingly, Jordan in combination with Barclay would yield a device with a water insoluble outer layer, not a layer which dissolves or disperses in the mouth.

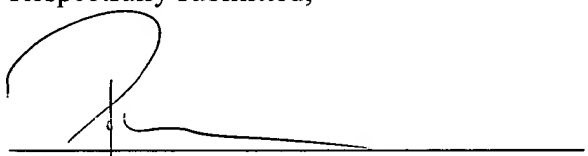
Faour

Faour describes and claims a multi-layer osmotic delivery device (col. 4, lines 63-66). The device requires a first agent containing core surrounded by a semipermeable membrane (col. 4, line 66 to col. 5, line 6). The first active agent is released through a preformed passageway in the semipermeable membrane which is generated by mechanical perforation, laser perforation or any other similar method (col. 8, lines 58-61). The outer layer does not dissolve or disperse in an aqueous environment, as required for a device which dissolves or disperses when applied to the buccal or sublingual areas of the mouth.

In combination, Barclay and Faour, et al. would not lead to the claimed device and method of manufacture, but to an osmotic device with a water-insoluble outer layer. Accordingly, Barclay and Faour in combination do not make obvious the claimed device or method of manufacture (*see*, *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986); *see also* MPEP § 2141).

Allowance of all claims 1-29 and 32 are earnestly solicited.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Date: October 10, 2002
Holland & Knight LLP
One Atlantic Center, Suite 2000
1201 W. Peachtree Street
Atlanta, GA 30309-3400
(404) 817 – 8473
(404) 817 – 8588 (fax)

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this Amendment and Response to Office Action, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Commissioner for Patents, P. O. Box 2327, Arlington, VA 22202.

Jean Hicks

Date: October 15, 2002

Appendix I: Marked-up copy of the amended claims as pending

1. (amended) A pharmaceutical composition in unit dosage form for both intraoral and oral administration to a patient, said unit dosage form configured to be placed within the mouth of said patient, which comprises:

(a) as a first portion, at least one discrete outer layer which dissolves or disintegrates, intraorally, the layer comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level; and

(b) as a second portion located within said first portion, a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestibile by the patient after the outer layer has disintegrated or has dissolved intraorally.

2. The pharmaceutical composition defined in claim 1 in the form of a tablet or capsule.

3. The pharmaceutical composition defined in claim 2 wherein the unit dosage form is a tablet and the second portion of the composition is an inner core or at least one layer of a multi-layer tablet, and the first portion is either an outer coating applied on the core or is one or more of the outer layers of a multi-layer tablet.

4. (amended) The pharmaceutical composition defined in claim 2 wherein the unit dosage form is a capsule and the second portion of the composition is an uncoated capsule including the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level on which the first portion is applied as an outer layer forming an outer coating.

5. The pharmaceutical composition defined in claim 3 wherein the outer coating is a film coat that is applied as a layer to the inner core.

6. The pharmaceutical composition defined in claim 3 wherein the outer coating is a compression coat that is compressed around the inner core.

7. (amended) The pharmaceutical composition defined in claim 5 wherein the film coat comprises the at least one pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level and at least one pharmaceutically acceptable coating polymer selected from the group consisting of cellulose, hydroxypropyl methylcellulose, methyl cellulose, polyvinylpyrrolidone, and polyethylene glycol, a pharmaceutically acceptable plasticizer, a pharmaceutically acceptable glidant and a pharmaceutically acceptable colorant.

8. (amended) The pharmaceutical composition defined in claim 6 wherein the compression coat comprises the at least one pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level and at least one pharmaceutically acceptable excipient for intraoral administration of the pharmaceutically active ingredient.

9. (amended) The pharmaceutical composition defined in claim 6 wherein the compression coat comprises the at least one pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level formulated in a pharmaceutically acceptable effervescent agent which generates effervescence when contacted with salivary fluid.

10. (amended) The pharmaceutical composition defined in claim 3 wherein the first portion comprises one or two outer layers each comprising a therapeutically effective

amount of at least one pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level and one or more pharmaceutically acceptable excipients for intraoral administration of the pharmaceutically active ingredient capable of[intraoral administration] sublingual or buccal absorption in a therapeutically effective level.

11. (amended) The pharmaceutical composition defined in claim 3 wherein the outer layer of the multi-layer tablet is formulated with a pharmaceutically acceptable effervescent agent which [generated] generates effervescence when contacted with salivary fluid.

12. The pharmaceutical composition defined in claim 7 wherein the film coat further comprises a pharmaceutically acceptable flavoring agent.

13. (amended) The pharmaceutical composition defined in claim 3 wherein the inner core is an immediate drug release tablet comprising the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level and at least one pharmaceutically acceptable excipients for oral administration of the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level.

14. (amended) The pharmaceutical composition defined in claim 3 wherein the inner core is in a configuration which provides sustained release of the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level and which further provides an immediate drug release layer tablet comprising the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level and at least one

pharmaceutically acceptable excipient for oral administration of the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level.

15. (amended) The pharmaceutical composition defined in claim 3 wherein the second portion is the at least one layer of the multi-layer tablet comprising the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level and which is an immediate drug release layer.

16. (amended) The pharmaceutical composition defined in claim 3 wherein the second portion is the at least one inner layer and provides sustained release of the pharmaceutically active ingredient suitable for [oral administration] sublingual or buccal absorption in a therapeutically effective level over a period of 0.5 to 24 hours.

17. (amended) The pharmaceutical composition defined in claim 3 wherein a delayed release coating covers the inner core and comprises the second portion of the composition and then the first portion of the composition is an outer layer over the delayed release coating to delay release of the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level for a period of 0.5 to 12 hours.

18. The pharmaceutical composition defined in claim 17 wherein the delayed release coating comprises one or more pharmaceutically acceptable polymer selected from the group consisting of methyl cellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxymethyl cellulose, hydroxypropyl methyl cellulose acetate succinate, ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, cellulose

acetate trimellitate, carboxymethylcellulose sodium, acrylic acid polymers and copolymers, polymers or copolymers of methacrylic acid, methyl acrylate, ethyl acrylate, methyl methacrylate, ethyl methacrylate, vinyl acetate, vinyl acetate phthalate, or an azo compound, polyvinyl pyrrolidone, pectin, amylase, shellac, zein, and guar gum.

19. The pharmaceutical composition defined in claim 3 wherein the inner core or a layer of the multi-layer table core is chewable and comprises at least one pharmaceutically acceptable excipient suitable for a chewable medication and a flavoring agent.

20. The pharmaceutical composition defined in claim 4 wherein the film coat comprises the pharmaceutically active ingredient capable of intraoral administration and at least one pharmaceutically acceptable coating polymer selected from the group consisting of cellulose, hydroxypropyl methylcellulose, methyl cellulose, polyvinyl pyrrolidone, and polyethylene glycol, a pharmaceutically acceptable plasticizer, a pharmaceutically acceptable glidant, a pharmaceutically acceptable colorant, and optionally a pharmaceutically acceptable flavoring agent.

21. (amended) The pharmaceutical composition defined in claim 4 wherein the second portion of the composition is a capsule containing the pharmaceutically active ingredient capable of [oral administration] <u>sublingual or buccal absorption in a therapeutically effective level</u> and a pharmaceutically acceptable excipient for sustained release of the pharmaceutically active ingredient suitable for [oral administration] <u>sublingual or buccal absorption in a therapeutically effective level</u> to provide a sustained release effect of the pharmaceutically active ingredient for 0.5 to 24 hours.

22. (amended) The pharmaceutical composition defined in claim 1 wherein the outer layer disintegrates or dissolves within 10 minutes [permitting release of the pharmaceutically active ingredient capable of intraoral administration], when the composition is contacted with saliva during intraoral administration.

23. (amended) The pharmaceutical composition defined in claim 22 wherein the second part of the composition containing the pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level remains intact until the intraoral administration of the pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level has been completed.

24. (amended) The pharmaceutical composition defined in claim 22 wherein the outer layer disintegrates immediately to allow a rapid intraoral mucosal absorption of the pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level released from the outer layer.

25. (amended) The pharmaceutical composition defined in claim 1 which further comprises a pharmaceutically acceptable signaling system located between the first portion and second portion of the composition, within the first portion of the composition or within the second portion of the composition and that is detectable by the patient upon substantial release of the pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level during intraoral administration thereby informing the patient that it is time to [orally ingest] chew or swallow the remaining second part of the composition containing the

pharmaceutically active ingredient capable of [oral administration] sublingual or buccal absorption in a therapeutically effective level.

26. (amended) The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level is metabolized in [has] a first pass [metabolism] which is avoided by intraoral administration.

27. (amended) The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level has a rapid onset of desired therapeutic effect through [intraoral absorption] sublingual or buccal absorption.

28. (amended) The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level is selected from the group consisting of analgesics, antihistamines, antidiarrheals, anxiolytics, hypnotics, stimulants, cardiovascular drugs, pulmonary drugs, anti-hypertensives, anti-emetics, anti-inflammatory drugs, renal drugs, steroids, drugs for neurological disorders, anti-psychotic drugs, drugs for treating endocrine disorders, drugs for promoting immunology, drugs for treating osteoarthritis, drugs for treating glaucoma, drugs for treating allergic rhinitis, drugs for treating anemias and other hematological disorders, drugs for treating infectious diseases, drugs for the treatment and symptoms of cancer, drugs for insomnia, and antidiabetic drugs.

29. (amended) A process for the preparation of a pharmaceutical composition in unit dosage form as a tablet or capsule for both intraoral and oral administration to a patient,

said pharmaceutical composition placed within the mouth of said patient, which comprises:

(a) as a first portion, at least one discrete outer layer which dissolves or disintegrates, intraorally, the layer comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level; and

(b) as a second portion located within said first portion, a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the at least one outer layer has disintegrated or has dissolved within the patient's mouth which comprises the steps of:

(i) providing the second portion as an inner tablet core or as at least one layer of a multi-layer tablet core or as an uncoated capsule; and

(ii) applying the first portion as an outer layer or as several outer layers forming an outer coating on the first portion.

Please cancel claims 30 and 31.

32. (amended) An analgesic pharmaceutical composition in unit dosage form as a tablet for both intraoral and oral administration to a patient, said unit dosage form configured to be placed within the mouth of said patient and has an outer coating which disintegrates or dissolves in the patient's mouth, which comprises:

(a) as a first portion, or at least one discrete outer layer which dissolves or disintegrates, intraorally, the layer comprising a therapeutically effective amount of

butorphanol tartrate capable of [intraoral administration] sublingual or buccal absorption in a therapeutically effective level;

(b) as a second portion located within said first portion, a therapeutically effective amount of rofecoxib capable of oral administration and which is releasable and orally ingestible by the patient after the outer layer has disintegrated or has dissolved intraorally; and

(c) a pharmaceutically acceptable signaling system located between the first portion and second portion of the composition, within the first portion of the composition or within the second portion of the composition and that is detectable by the patient upon substantial release of the butorphanol tartrate capable of intraoral administration during intraoral administration thereby informing the patient that it is time to orally ingest the remaining second part of the composition containing the rofecoxib capable of oral administration.

Appendix II: Clean copy of the amended claims as pending

1. (amended) A pharmaceutical composition in unit dosage form for both intraoral and oral administration to a patient, said unit dosage form configured to be placed within the mouth of said patient, which comprises:

(a) as a first portion, at least one discrete outer layer which dissolves or disintegrates, intraorally, the layer comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level; and

(b) as a second portion located within said first portion, a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestibile by the patient after the outer layer has disintegrated or has dissolved intraorally.

2. The pharmaceutical composition defined in claim 1 in the form of a tablet or capsule.

3. The pharmaceutical composition defined in claim 2 wherein the unit dosage form is a tablet and the second portion of the composition is an inner core or at least one layer of a multi-layer tablet, and the first portion is either an outer coating applied on the core or is one or more of the outer layers of a multi-layer tablet.

4. (amended) The pharmaceutical composition defined in claim 2 wherein the unit dosage form is a capsule and the second portion of the composition is an uncoated capsule including the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level on which the first portion is applied as an outer layer forming an outer coating.

5. The pharmaceutical composition defined in claim 3 wherein the outer coating is a film coat that is applied as a layer to the inner core.

6. The pharmaceutical composition defined in claim 3 wherein the outer coating is a compression coat that is compressed around the inner core.

7. (amended) The pharmaceutical composition defined in claim 5 wherein the film coat comprises the at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and at least one pharmaceutically acceptable coating polymer selected from the group consisting of cellulose, hydroxypropyl methylcellulose, methyl cellulose, polyvinylpyrrolidone, and polyethylene glycol, a pharmaceutically acceptable plasticizer, a pharmaceutically acceptable glidant and a pharmaceutically acceptable colorant.

8. (amended) The pharmaceutical composition defined in claim 6 wherein the compression coat comprises the at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and at least one pharmaceutically acceptable excipient for intraoral administration of the pharmaceutically active ingredient.

9. (amended) The pharmaceutical composition defined in claim 6 wherein the compression coat comprises the at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level formulated in a pharmaceutically acceptable effervescent agent which generates effervescence when contacted with salivary fluid.

10. (amended) The pharmaceutical composition defined in claim 3 wherein the first portion comprises one or two outer layers each comprising a therapeutically effective

amount of at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and one or more pharmaceutically acceptable excipients for intraoral administration of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level.

11. (amended) The pharmaceutical composition defined in claim 3 wherein the outer layer of the multi-layer tablet is formulated with a pharmaceutically acceptable effervescent agent which generates effervescence when contacted with salivary fluid.

12. The pharmaceutical composition defined in claim 7 wherein the film coat further comprises a pharmaceutically acceptable flavoring agent.

13. (amended) The pharmaceutical composition defined in claim 3 wherein the inner core is an immediate drug release tablet comprising the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and at least one pharmaceutically acceptable excipients for oral administration of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level.

14. (amended) The pharmaceutical composition defined in claim 3 wherein the inner core is in a configuration which provides sustained release of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and which further provides an immediate drug release layer tablet comprising the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and at least one pharmaceutically acceptable excipient for oral administration of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level.

15. (amended) The pharmaceutical composition defined in claim 3 wherein the second portion is the at least one layer of the multi-layer tablet comprising the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and which is an immediate drug release layer.

16. (amended) The pharmaceutical composition defined in claim 3 wherein the second portion is the at least one inner layer and provides sustained release of the pharmaceutically active ingredient suitable for sublingual or buccal absorption in a therapeutically effective level over a period of 0.5 to 24 hours.

17. (amended) The pharmaceutical composition defined in claim 3 wherein a delayed release coating covers the inner core and comprises the second portion of the composition and then the first portion of the composition is an outer layer over the delayed release coating to delay release of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level for a period of 0.5 to 12 hours.

18. The pharmaceutical composition defined in claim 17 wherein the delayed release coating comprises one or more pharmaceutically acceptable polymer selected from the group consisting of methyl cellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxymethyl cellulose, hydroxypropyl methyl cellulose acetate succinate, ethyl cellulose, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, cellulose acetate trimellitate, carboxymethylcellulose sodium, acrylic acid polymers and copolymers, polymers or copolymers of methacrylic acid, methyl acrylate, ethyl acrylate, methyl methacrylate, ethyl methacrylate, vinyl acetate, vinyl acetate phthalate, or an azo compound, polyvinyl pyrrolidone, pectin, amylase, shellac, zein, and guar gum.

19. The pharmaceutical composition defined in claim 3 wherein the inner core or a layer of the multi-layer table core is chewable and comprises at least one pharmaceutically acceptable excipient suitable for a chewable medication and a flavoring agent.

20. The pharmaceutical composition defined in claim 4 wherein the film coat comprises the pharmaceutically active ingredient capable of intraoral administration and at least one pharmaceutically acceptable coating polymer selected from the group consisting of cellulose, hydroxypropyl methylcellulose, methyl cellulose, polyvinyl pyrrolidone, and polyethylene glycol, a pharmaceutically acceptable plasticizer, a pharmaceutically acceptable glidant, a pharmaceutically acceptable colorant, and optionally a pharmaceutically acceptable flavoring agent.

21. (amended) The pharmaceutical composition defined in claim 4 wherein the second portion of the composition is a capsule containing the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level and a pharmaceutically acceptable excipient for sustained release of the pharmaceutically active ingredient suitable for sublingual or buccal absorption in a therapeutically effective level to provide a sustained release effect of the pharmaceutically active ingredient for 0.5 to 24 hours.

22. (amended) The pharmaceutical composition defined in claim 1 wherein the outer layer disintegrates or dissolves within ~~10 minutes~~, when the composition is contacted with saliva during intraoral administration.

23. (amended) The pharmaceutical composition defined in claim 22 wherein the second part of the composition containing the pharmaceutically active ingredient capable

of sublingual or buccal absorption in a therapeutically effective level remains intact until the intraoral administration of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level has been completed.

24. (amended) The pharmaceutical composition defined in claim 22 wherein the outer layer disintegrates immediately to allow a rapid intraoral mucosal absorption of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level released from the outer layer.

25. (amended) The pharmaceutical composition defined in claim 1 which further comprises a pharmaceutically acceptable signaling system located between the first portion and second portion of the composition, within the first portion of the composition or within the second portion of the composition and that is detectable by the patient upon substantial release of the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level during intraoral administration thereby informing the patient that it is time to chew or swallow the remaining second part of the composition containing the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level.

26. (amended) The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level is metabolized in a first pass which is avoided by intraoral administration.

27. (amended) The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of sublingual or buccal absorption in a

therapeutically effective level has a rapid onset of desired therapeutic effect through sublingual or buccal absorption.

28. (amended) The pharmaceutical composition defined in claim 1 wherein the pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level is selected from the group consisting of analgesics, antihistamines, antidiarrheals, anxiolytics, hypnotics, stimulants, cardiovascular drugs, pulmonary drugs, anti-hypertensives, anti-emetics, anti-inflammatory drugs, renal drugs, steroids, drugs for neurological disorders, anti-psychotic drugs, drugs for treating endocrine disorders, drugs for promoting immunology, drugs for treating osteoarthritis, drugs for treating glaucoma, drugs for treating allergic rhinitis, drugs for treating anemias and other hematological disorders, drugs for treating infectious diseases, drugs for the treatment and symptoms of cancer, drugs for insomnia, and antidiabetic drugs.

29. (amended) A process for the preparation of a pharmaceutical composition in unit dosage form as a tablet or capsule for both intraoral and oral administration to a patient, said pharmaceutical composition placed within the mouth of said patient, which comprises:

(a) as a first portion, at least one discrete outer layer which dissolves or disintegrates, intraorally, the layer comprising a therapeutically effective amount of at least one pharmaceutically active ingredient capable of sublingual or buccal absorption in a therapeutically effective level; and

(b) as a second portion located within said first portion, a therapeutically effective amount of at least one pharmaceutically active ingredient capable of oral administration and which is releasable and orally ingestible by the patient after the at

least one outer layer has disintegrated or has dissolved within the patient's mouth which comprises the steps of:

(i) providing the second portion as an inner tablet core or as at least one layer of a multi-layer tablet core or as an uncoated capsule; and

(ii) applying the first portion as an outer layer or as several outer layers forming an outer coating on the first portion.

Please cancel claims 30 and 31.

32. (amended) An analgesic pharmaceutical composition in unit dosage form as a tablet for both intraoral and oral administration to a patient, said unit dosage form configured to be placed within the mouth of said patient and has an outer coating which disintegrates or dissolves in the patient's mouth, which comprises:

(a) as a first portion, or at least one discrete outer layer which dissolves or disintegrates, intraorally, the layer comprising a therapeutically effective amount of butorphanol tartrate capable of sublingual or buccal absorption in a therapeutically effective level;

(b) as a second portion located within said first portion, a therapeutically effective amount of rofecoxib capable of oral administration and which is releasable and orally ingestible by the patient after the outer layer has disintegrated or has dissolved intraorally; and

(c) a pharmaceutically acceptable signaling system located between the first portion and second portion of the composition, within the first portion of the composition or within the second portion of the composition and that is detectable by the patient upon substantial release of the butorphanol tartrate capable of intraoral administration during

intraoral administration thereby informing the patient that it is time to orally ingest the remaining second part of the composition containing the rofecoxib capable of oral administration.

Bld Cont